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Dear Editor

The Pitfalls of FeNO Testing

The article on fractional exhaled nitric oxide (FeNO) as a marker of airway inflammation by Mitsuru Munakata[1] correctly highlights the practical problems clinicians face when interpreting the FeNO results in the clinic due to (a) large variations in the 'normal' ranges of FeNO in children and adults (usual upper limit of reference range 27-57 parts per billion by volume [ppbv] excluding asthma and atopy but still dependent on gender)[2]; (b) different technologies in use to measure the FeNO levels such as with the electrochemical sensor NIOX MINO® portable handheld NO analyzer (Aerocrine AB, Stockholm, Sweden) assuming a constant flow rate of 50 ml/s, or the more sensitive and NO specific but labour-intensive chemiluminescence method and emerging technology such as the quantum cascade laser (QSL) method reaching detection sensitivity at single part per billion by volume (ppbv, $1 : 10^{-9}$).[3] Of note, The National Health and Nutrition Examination Survey report just published data on 13,275 participants aged six to 80 years who had their FeNO measured using the chemiluminescence method also show the large variations that remain to be explained,[4] apart from gender, atopy, smoking and paranasal sinus inflammation that are known factors to affect results.

One group of clinical conditions where persistent low values <25 ppbv in adults and <20 ppbv in children are extremely significant is ciliary problems, especially primary ciliary dyskinesia (PCD) where low FeNO is reportedly highly sensitive 97% and specific 90% for this condition.[5] A diagnosis of airway inflammation (eosinophilic or otherwise) is unlikely if FeNO levels are always low and ciliary dyskinesias especially if bronchiectasis if present should be considered. It remains to be established whether local inducible nitric oxide synthase (iNOS) is affected in PCD as a generalized disorder of NO handling has not been demonstrated.[6] Clinicians therefore need to know the limitations of biologic tests and follow up persistently low FeNO levels and question the diagnosis of airway inflammation in these patients.

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